

## A Novel Determinant of Prognosis in Acute Pulmonary Edema: Intermountain Risk Score

### Akut Akciğer Ödeminde Prognozun Yeni Bir Belirleyicisi: Intermountain Risk Skoru

#### ABSTRACT

**Objective:** The Intermountain Risk Score (IMRS), calculated using age, gender, complete blood count (CBC), and simple laboratory analyses, is an easy-to-use and cost-effective tool developed to predict mortality. In our study, we aimed to determine whether the IMRS could predict mortality in patients admitted to the hospital with a diagnosis of acute pulmonary edema.

**Methods:** A total of 371 patients who were admitted with a diagnosis of pulmonary edema, were included in our study. The IMRS of the patients was determined using a calculation tool, and the patients were divided into three groups based on the determined value: low, moderate, and high IMRS.

**Results:** The patients included in our study comprised 208 women and 163 men, with an average age of 68.7 years. There was a statistically significant difference between the patient groups concerning both 1-month and 1-year mortality rates. Additionally, there was a significant difference in IMRS between patients who developed in-hospital, 1-month, and 1-year mortality and those who survived. In the Receiver Operating Characteristic (ROC) analysis, a cutoff value of 15.5 for the IMRS predicted both 1-year and 1-month mortality. In the Kaplan-Meier analysis, the highest mortality risk was observed in the high IMRS group and the lowest mortality risk in the low IMRS group.

**Conclusion:** Our research results show that the IMRS strongly predicts both short-term and long-term mortality in patients hospitalized with a diagnosis of acute pulmonary edema.

**Keywords:** Acute pulmonary edema, intermountain risk score, mortality

#### ÖZET

**Amaç:** Yaş ve cinsiyet parametrelerinin yanı sıra tam kan sayımı ve bazı basit laboratuvar analizleri kullanılarak hesaplanan Intermountain Risk Skoru (IMRS), kullanımı basit ve ucuz olup mortaliteyi tahmin etmek amacıyla geliştirilmiştir. Çalışmamızda akut akciğer ödemi tanısıyla hastaneye başvuran hastalarda IMRS'nin mortaliteyi tahmin edip edemeyeceğini belirlemeyi amaçladık.

**Yöntemler:** Çalışmamıza akciğer ödemi tanısıyla başvuran 371 hasta dahil edildi. Hastaların IMRS'leri hesaplama aracı kullanılarak belirlendi ve hastalar belirlenen değere göre düşük, orta ve yüksek IMRS olmak üzere üç gruba ayrıldı.

**Bulgular:** Çalışmamıza dahil edilen hastaların 208'i kadın, 163'ü erkek olup yaş ortalaması 68,7 idi. Hasta grupları arasında hem 1 aylık hem de 1 yıllık mortalite oranları açısından istatistiksel olarak anlamlı farklılık vardı. Ayrıca hastane içi, 1 aylık ve 1 yıllık mortalite gelişen hastalar ile hayatta kalanlar arasında IMRS açısından anlamlı fark vardı. ROC analizinde IMRS için kesme noktasının 15,5 olması hem 1 yıllık hem de 1 aylık mortaliteyi öngörüyordu. Kaplan-Meier analizinde en yüksek mortalite riski IMRS yüksek grupta, en düşük mortalite riski ise IMRS düşük grupta gözlemlendi.

**Sonuç:** Araştırma sonuçlarımız, IMRS'nin akut akciğer ödemi tanısıyla hastaneye yatırılan hastalarda hem kısa hem de uzun vadeli mortaliteyi güçlü bir şekilde öngördüğünü göstermektedir.

**Anahtar Kelimeler:** Akut akciğer ödemi, intermountain risk skoru, mortalite

#### ORIGINAL ARTICLE

#### KLİNİK ÇALIŞMA

Raif Kılıç<sup>1</sup> 

Adem Aktan<sup>2</sup> 

Tuncay Güzel<sup>3</sup> 

Ahmet Ferhat Kaya<sup>4</sup> 

Hamdullah Güzel<sup>5</sup> 

Bayram Arslan<sup>6</sup> 

Mehmet Ali Işık<sup>6</sup> 

Mehmet Sait Coşkun<sup>7</sup> 

Yusuf Çankaya<sup>8</sup> 

<sup>1</sup>Department of Cardiology, Çermik State Hospital, Diyarbakır, Türkiye

<sup>2</sup>Department of Cardiology, Mardin Artuklu University Medical Faculty, Mardin, Türkiye

<sup>3</sup>Department of Cardiology, Health Science University, Gazi Yaşargil Training and Research Hospital, Diyarbakır, Türkiye

<sup>4</sup>Department of Cardiology, Muş State Hospital, Muş, Türkiye

<sup>5</sup>Department of Cardiology, Düzce University Faculty of Medicine, Düzce, Türkiye

<sup>6</sup>Department of Cardiology, Mardin Training and Research Hospital, Mardin, Türkiye

<sup>7</sup>Department of Cardiology, Ergani State Hospital, Diyarbakır, Türkiye

<sup>8</sup>Department of Emergency Medicine, Çermik State Hospital, Diyarbakır, Türkiye

#### Corresponding author:

Raif Kılıç

✉ raifklic@hotmail.com

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Acute pulmonary edema is defined as a sudden increase in fluid in the interstitial and/or alveolar spaces of the lung parenchyma.<sup>1</sup> Patients usually present with dyspnea at rest.<sup>2</sup> The clinical condition of patients worsens in the presence of tachycardia, hypoxemia, and tachypnea. Patients are usually hypertensive due to stress and increased endogenous catecholamine release, but may also be hypotensive in cardiogenic shock.<sup>3</sup> In the treatment of acute pulmonary edema, vasodilators and nitrates are used for hypervolemia, while non-invasive or invasive ventilation may be required for refractory hypoxemia.<sup>2,4</sup>

While in-hospital mortality in patients who develop acute pulmonary edema ranges between 4-10%, 1-year mortality increases to 25-30%.<sup>5,6</sup> Therefore, predicting mortality is critical for closely monitoring these patients. In 2009, Horne et al.<sup>7</sup> introduced the Intermountain Risk Score (IMRS) to assess the risk of all-cause mortality in the general population. This score, which is simple and inexpensive to use, includes parameters such as age, gender, complete blood count (CBC), and basic laboratory analyses. The IMRS has been studied as a prognostic factor for both short- and long-term survival, particularly in patients diagnosed with heart failure.<sup>7,8</sup> Additionally, the IMRS was examined in patients undergoing transcatheter aortic valve implantation (TAVI), with higher values predicting long-term mortality.<sup>9</sup> Lastly, the impact of the IMRS on prognosis in patients with ST-elevation myocardial infarction (STEMI) was explored, showing its ability to predict both short- and long-term outcomes.<sup>10</sup>

Our study aims to determine whether the IMRS can predict mortality for patients admitted with acute pulmonary edema during hospitalization, the first month, and the first year.

## Materials and Methods

This retrospective analysis included patients who presented to three centers with a diagnosis of pulmonary edema and were hospitalized between January 1, 2020 and June 1, 2022. The diagnosis of acute pulmonary edema was based on the guidelines for heart failure from the European Society of Cardiology (ESC).<sup>11</sup> Patient records at the time of hospital admission were reviewed. The study included individuals aged 18 years and older who were diagnosed with acute

pulmonary edema according to current guidelines, were admitted to the intensive care unit, and had complete records. Patients with active infections, advanced liver and kidney failure, cardiogenic shock at the time of admission, cancer, autoinflammatory diseases, marked anemia, and missing data at the time of admission were excluded from the study. Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Mardin Artuklu University (Approval Number: 2023/10-8, Date: 09.10.2023).

The patients' IMRS risk score was determined using the calculation tool available on the Intermountain Healthcare website (<https://intermountainhealthcare.org/IMRS/>). This calculation tool includes the following parameters: hematocrit, sodium, potassium, white blood cell count, platelet count, mean platelet volume, mean corpuscular hemoglobin concentration, red cell distribution width, mean corpuscular volume, glucose, creatinine, bicarbonate, calcium, age, and gender. The laboratory values of the patients at their initial admission were used to calculate the IMRS. The IMRS was categorized as low, moderate, and high.<sup>12</sup> The IMRS classifications are as follows:

- Female: < 9 low, 9-14 moderate, > 14 high
- Male: 11 < low, 11-16 moderate, > 16 high.

Patient demographic variables including gender, age, body mass index (BMI), chronic renal insufficiency, chronic obstructive pulmonary disease, diabetes, ischemic heart disease, and hypertension at the time of admission to the hospital were recorded. Echocardiography and biochemical parameters, complete blood count, blood gas analysis, and lipid profile were examined at the time of admission. The primary endpoints of the study were in-hospital, 1-month, and 1-year mortality. The data on the patients were obtained from the hospitals' digital databases and the national registry system. Artificial intelligence (AI)-enabled technologies, such as Large Language Models (LLMs), chatbots, or image generators, were not used in the preparation of this manuscript.

## Statistical Analysis

Statistical analysis was conducted using SPSS 22.0 (IBM Corp., Armonk, New York, USA) software. The Kolmogorov-Smirnov test was used to evaluate whether continuous variables were normally distributed. For normally distributed variables, Student's t-test was used for comparisons between two groups, and Analysis of Variance (ANOVA) was used for comparisons among more than two groups. For non-normally distributed variables, the Mann-Whitney U test was used for comparisons between two groups, and the Kruskal-Wallis test was used for comparisons among more than two groups. Receiver operating characteristic (ROC) analysis was used to test the ability of the IMRS score to predict 1-year mortality and to determine a cut-off value based on the highest sum of sensitivity and specificity. Kaplan-Meier analysis was used to evaluate the probability of 1-year survival among patients with different IMRS classes. A p-value < 0.05 was considered statistically significant.

## ABBREVIATIONS

BI-EFFECT	Biomarker Enhanced International Acute Heart Failure
BMI	Body mass index
BNP	B-type natriuretic peptide
CBC	Complete blood count
CRP	C-reactive protein
EF	Ejection fraction
EFFECT	Enhanced Feedback for Effective Cardiac Treatment
ESC-HF-LT	European Society of Cardiology Heart Failure Long-Term
IMRS	Intermountain Risk Score
IN-HF	International Network for Heart Failure
MOCA	Measurement of Clinical and Angiographic Outcomes
NT-proBNP	N-terminal pro b-type natriuretic peptide
ROC	Receiver Operating Characteristic
STEMI	ST-elevation myocardial infarction
TAVI	Transcatheter aortic valve implantation

## Results

Our study included 371 patients, comprising 208 women and 163 men, with an average age of 68.7 years. Patients were divided into three groups according to their IMRS classifications: low, moderate, and high. The ejection fraction (EF) was significantly different across patient groups ( $42.1 \pm 13.2$ ,  $38.3 \pm 12.1$ ,  $36.6 \pm 12.7$ ;  $P = 0.014$ , respectively). Additionally, significant differences were observed between the groups in terms of white blood cell (WBC) count and C-reactive protein (CRP) levels ( $14.1 \pm 3.9$ ,  $14.9 \pm 3.8$ ,  $16.1 \pm 5.9$ ;  $P = 0.012$  and  $27.9 \pm 17.3$ ,  $30.5 \pm 22.0$ ,  $36.3 \pm 19.7$ ;  $P = 0.006$ , respectively). Statistically significant differences were also noted in both 1-month and 1-year mortality rates (1<sup>st</sup> month

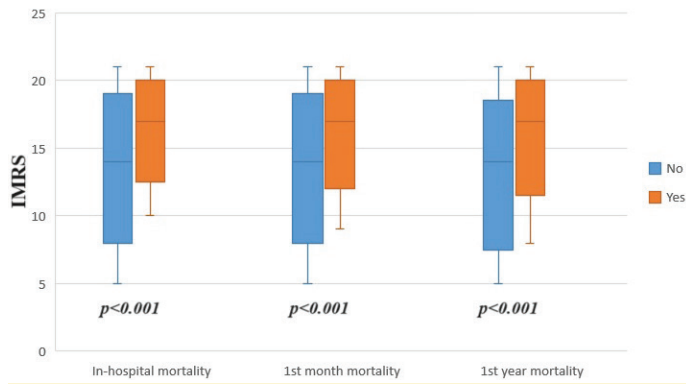
mortality: 3 (4.9%), 9 (6.3%), 23 (13.8%);  $P = 0.034$ , and 1<sup>st</sup> year mortality: 5 (8.2%), 20 (14.0%), 47 (28.1%);  $P < 0.001$ , respectively). However, there was no statistical difference in in-hospital mortality rates [1 (1.6%), 5 (3.5%), 12 (7.2%);  $P = 0.142$ , respectively]. No statistically significant differences were observed in other characteristics between IMRS classes. The basic demographic characteristics of the patients according to IMRS class are summarized in Table 1.

There was a significant difference in the IMRS scores between patients with in-hospital, 1-month, and 1-year mortality and those who survived (in-hospital: 14.0 (11.0-17.0) versus 17.0 (15.7-19.2);  $P < 0.001$ , 1<sup>st</sup> month: 14.0 (11.0-17.0) versus 17.0 (15.0-19.0);  $P < 0.001$ , 1<sup>st</sup> year: 14.0 (10.0-16.0) versus

**Table 1. Basic Demographic Characteristics of Patients According to the Intermountain Risk Score (IMRS) Classes**

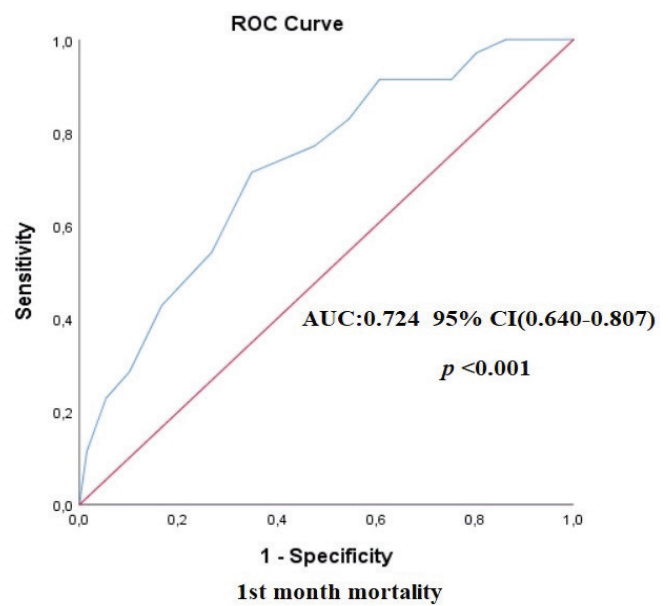
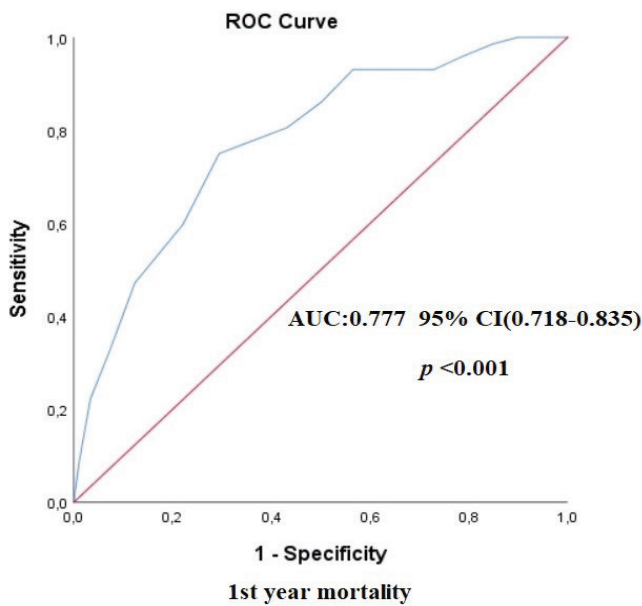
	Low IMRS n = 61	Moderate IMRS n = 143	High IMRS n = 167	P
Gender (Female), n (%)	29 (47.5)	80 (55.9)	99 (59.3)	0.286
Age, (years)	67.9 ± 9.2	69.3 ± 8.5	68.4 ± 8.6	0.494
Body Mass Index, (kg/m <sup>2</sup> )	26.1 ± 3.7	26.5 ± 3.2	26.2 ± 3.5	0.587
Heart Rate (per minute)	85.5 ± 16.2	86.6 ± 18.2	87.9 ± 18.9	0.654
Systolic Blood Pressure (mmHg)	171.5 ± 26.7	173.8 ± 26.8	176.2 ± 27.4	0.463
Diastolic Blood Pressure (mmHg)	100.0 ± 14.8	100.4 ± 14.7	101.4 ± 15.4	0.714
Ischemic CMP, n (%)	25 (41.0)	61 (42.7)	76 (45.5)	0.791
COPD, n (%)	13 (21.3)	34 (23.8)	38 (22.8)	0.927
GFR, (mL/min)	59.0 (32.5-68.5)	56.0 (30.0-68.0)	52.0 (29.0-70.0)	0.885
BUN, (mg/dL)	36.3 ± 16.8	37.8 ± 17.3	38.6 ± 18.5	0.691
Creatinine, (mg/dL)	1.00 (0.76-1.37)	1.00 (0.78-1.30)	1.01 (0.79-1.60)	0.415
CRF, n (%)	32 (52.5)	81 (56.6)	99 (59.3)	0.646
HT, n (%)	43 (70.5)	98 (68.5)	122 (73.1)	0.681
DM, n (%)	14 (23.0)	32 (22.4)	44 (26.3)	0.695
EF, (%)	42.1 ± 13.2	38.3 ± 12.1	36.6 ± 12.7	<b>0.014</b>
Heart Failure Type, n (%)				
HFrEF	34 (55.7)	96 (67.1)	118 (70.7)	0.191
HFmrEF	4 (6.6)	10 (7.0)	13 (7.8)	
HFpEF	23 (37.7)	37 (25.9)	36 (21.6)	
Albumin (g/dL)	3.8 ± 0.7	4.0 ± 0.6	3.9 ± 0.7	0.196
Hgb (g/dL)	13.0 ± 2.1	12.9 ± 1.6	12.6 ± 1.7	0.175
Hct (%)	40.2 ± 5.1	39.4 ± 4.5	39.0 ± 5.0	0.234
Plt (10 <sup>3</sup> /uL)	197 (161-276)	226 (180-261)	215 (172-266)	0.396
WBC (x10 <sup>3</sup> /uL)	14.1 ± 3.9	14.9 ± 3.8	16.1 ± 5.9	<b>0.012</b>
CRP (mg/dL)	27.9 ± 17.3	30.5 ± 22.0	36.3 ± 19.7	<b>0.006</b>
Glucose (mg/dL)	113.0 ± 33.0	113.5 ± 36.7	117.6 ± 42.8	0.574
In-Hospital Mortality	1 (1.6)	5 (3.5)	12 (7.2)	0.142
1 <sup>st</sup> Month Mortality	3 (4.9)	9 (6.3)	23 (13.8)	<b>0.034</b>
1 <sup>st</sup> Year Mortality	5 (8.2)	20 (14.0)	47 (28.1)	<b>&lt;0.001</b>

BUN, Blood Urea Nitrogen; CMP, Cardiomyopathy; COPD, Chronic Obstructive Pulmonary Disease; CRF, Chronic Renal Failure; CRP, C-Reactive Protein; DM: Diabetes Mellitus; EF, Ejection Fraction; GFR, Glomerular Filtration Rate; Hct, Hematocrit; HfmrEF, Heart Failure with Mildly Reduced Ejection Fraction; HFrEF, Heart Failure with Reduced Ejection Fraction; HFpEF, Heart Failure with Preserved Ejection Fraction; Hgb, Hemoglobin; HT, Hypertension; Plt: Platelet; WBC: White Blood Cell.

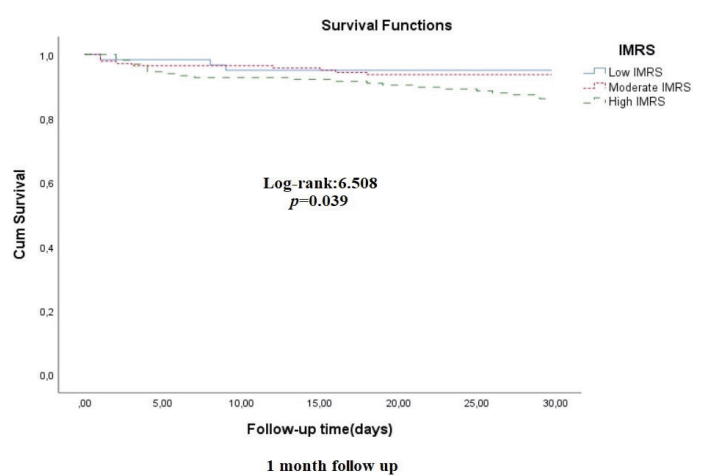
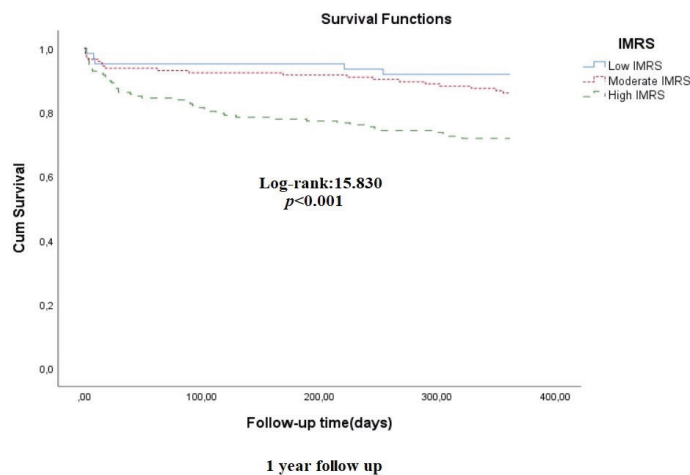


**Figure 1. Comparison of Intermountain Risk Score (IMRS) scores between patients who developed in-hospital, 1-month, and 1-year mortality and those who did not, as depicted in a box plot graphic.**

17.0 (15.2–19.0);  $P < 0.001$ , respectively) (Figure 1). In the ROC analysis, the cut-off point for the IMRS score was 15.5, which predicted 1-year mortality with 75% sensitivity and 71% specificity, and 1-month mortality with 71% sensitivity and 66% specificity [(1<sup>st</sup> year mortality: area under the curve (AUC): 0.777, 95% Confidence Interval (CI): 0.718–0.835,  $P < 0.001$ ) and (1<sup>st</sup> month mortality: AUC: 0.724, 95% CI: 0.640–0.807,  $P < 0.001$ )] (Figure 2). Kaplan–Meier analysis was performed to examine the association of mortality with IMRS groups at 1-year and 1-month follow-up. According to this analysis, the highest mortality risk was observed in the group with a high IMRS, and the lowest mortality risk was observed in the group with a low IMRS (1 year: Log rank: 15.830,  $P < 0.001$  and 1 month: Log rank: 6.508,  $P = 0.039$ , respectively) (Figure 3).



**Figure 2. Receiver operating characteristic (ROC) curve analysis of IMRS score on 1-year and 1-month mortality in patients with acute pulmonary edema.**



**Figure 3. Kaplan–Meier analysis of mortality association between IMRS groups at 1-year and 1-month follow-up.**

## Discussion

In this study, there was a significant relationship between a high IMRS score and both short-term and long-term mortality in patients admitted to the hospital due to acute pulmonary edema. Patients in the high IMRS category had much higher 1-month and 1-year death rates compared to patients with lower IMRS categories. This finding reveals that the IMRS score is an important prognostic indicator that affects not only patients' chances of survival in the acute period but also their long-term prognosis. As patients with high IMRS scores experience worse outcomes, more aggressive treatment approaches and close follow-up may be required in their management. Moreover, an IMRS >15.5 seems to be a valuable marker for risk stratification of the patients with acute pulmonary edema. The high sensitivity and specificity of the IMRS provide important information to clinicians, especially in identifying high-risk patients and determining appropriate treatment and follow-up strategies.

Acute pulmonary edema is an alarming and potentially fatal condition characterized by the sudden onset of symptoms. These patients must be recognized quickly, and treatment must be started immediately. Predicting mortality in acute pulmonary edema is important for optimizing treatment and closer monitoring. In the International Network for Heart Failure (IN-HF) study, anemia, low systolic blood pressure, age, and renal dysfunction were found to predict 1-year mortality in patients with acute heart failure.<sup>13</sup> In the MOCA (Measurement of Clinical and Angiographic Outcomes) study, biomarkers such as ST2, MR-proADM, natriuretic peptides, and CRP predicted both short-term (1-month) and long-term (1-year) mortality.<sup>14</sup> In the European Society of Cardiology Heart Failure Long-Term (ESC-HF-LT) registry, factors such as age, aortic stenosis, chronic obstructive pulmonary disease, low systolic blood pressure, renal failure, low EF, diabetes, and liver dysfunction were predictors of 1-year mortality.<sup>15</sup> In the Biomarker Enhanced International Acute Heart Failure (BI-EFFECT) study, the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) and BI-EFFECT scores were found to predict 30-day mortality in patients with acute heart failure.<sup>16</sup> In our study, the IMRS score predicted in-hospital, 1-month, and 1-year mortality in patients with acute pulmonary edema. To our knowledge, this may be the first study to examine the IMRS in acute pulmonary edema.

The IMRS was developed to assess individual mortality risk based on the patient's metabolic profile and complete blood count.<sup>7</sup> In 2010, the IMRS score was enhanced by incorporating red cell distribution width.<sup>17</sup> May et al.<sup>18</sup> reported the results of a study in which they augmented the IMRS by incorporating additional parameters such as bilirubin, albumin, and white cell differential count to improve the predictive power of the risk score. The IMRS encompasses a broad spectrum of prevalent medical risks and is capable of predicting various conditions leading to mortality, including cardiac disorders.<sup>17</sup> Complex data requirements often make calculating clinical risk scores difficult. In contrast, the IMRS relies solely on data from common laboratory tests and is notable for its ease of calculation and accessibility. It incorporates female gender as a factor associated with a lower risk of overall mortality compared to male gender.<sup>7</sup> By offering a freely accessible web

calculator, the IMRS provides a practical and useful solution for a wide range of users.<sup>12</sup> These features make the IMRS a tool that can be quickly and effectively integrated into clinical practice. Johnson et al.<sup>19,20</sup> documented that the IMRS has robust predictive power for mortality in patients undergoing coronary artery bypass grafting and showed significant predictive value for mortality when patients with coronary artery disease were stratified by percutaneous or drug treatment.

In a study investigating patients who underwent TAVI, it was found that a high IMRS score predicted long-term mortality.<sup>9</sup> This shows that the IMRS has the capacity to predict not only short-term but also long-term outcomes. In a study by Engelsgerd et al.,<sup>8</sup> high IMRS was found to be closely associated with 1-month and 1-year mortality in patients hospitalized due to heart failure. These findings support that IMRS is a reliable prognostic tool in heart failure patients. Two recent studies have indicated that the IMRS score predicts both short-term and long-term mortality in patients experiencing ST-elevation myocardial infarction, as well as in those with STEMI complicated by cardiogenic shock.<sup>10,21</sup> This shows that IMRS is also an important predictive tool in serious cardiovascular events such as acute coronary syndromes.

The IMRS was developed using a diverse and comprehensive patient population representative of general demographics. Because of its broad applicability, cost-effectiveness, and rapid acquisition, IMRS offers significant advantages that can be easily integrated into clinical practice. These features make IMRS a valuable resource for the implementation of secondary preventive measures in patients suffering from acute pulmonary edema. Using this score allows a more accurate and detailed determination of patients' risk profiles. In this context, the integration of IMRS into clinical practice has the potential to improve patient outcomes and increase the effectiveness of healthcare services. Future studies may further expand the use of the IMRS in different patient populations and clinical conditions, thus consolidating the prognostic value of this tool.

## Limitations

Our study had a few limitations. Although patients were recruited from three centers, our study had a relatively small sample size and was retrospective in nature. We were not able to analyze the impact of fluctuating trends in patients' biochemical parameters on short- and long-term mortality. As B-type natriuretic peptide (BNP)/N-terminal pro B-type natriuretic peptide (NT-proBNP) tests were not performed in some patients at the time of hospital admission, this parameter could not be included in our study. As only all-cause mortality and only patients with acute pulmonary edema were examined the findings cannot be generalized to other clinical outcomes and other cases of heart failure.

## Conclusion

In our study, the IMRS score predicted both short- and long-term mortality in patients hospitalized with a diagnosis of acute pulmonary edema. The IMRS score utilizes basic parameters commonly observed at the initial presentation of patients, making it a simple and practical tool for healthcare professionals. There is a need to substantiate our findings with larger studies.



**Ethics Committee Approval:** Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Mardin Artuklu University (Approval Number: 2023/10-8, Date: 09.10.2023).

**Informed Consent:** All patients gave informed consent prior to participation.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – R.K., A.A., T.G.; Design – R.K., A.F.K.; Supervision – B.A., M.A.I.; Resource – R.K., M.S.C., Y.Ç.; Materials – R.K., T.G., B.A.; Data Collection and/or Processing – R.K., A.A., T.G.; Analysis and/or Interpretation – R.K., A.F.K.; Literature Review – R.K., H.G., Y.Ç.; Writing – R.K., T.G.; Critical Review – A.A., M.S.C., H.G.

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**Conflict of Interest:** The authors have no conflicts of interest to declare.

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